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Original Article

Multifocal perivascular epithelioid cell tumor of the uterus: report of one case and literature review

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Abstract: Background: The tumor with perivascular epithelioid cells (PEComa) is a rare mesenchymal tumor originating from a perivascular epithelioid cell line. The uterus is the most common location of PEComa, but multifocal lesions are rare. This study aimed to analyze the clinicopathologic and histochemical characteristics of uterine PEComa. Methods: 1 case of uterine PEComa was detected by H&E staining and immunohistochemical SP method. Results: The 41-year-old female patient was admitted to the hospital due to gynecologic ultrasonography which showed a substantial heterogeneous mass in the pelvic cavity. According to the microscopic features and immunohistochemical markers, the tumor was diagnosed as multifocal tumors with perivascular epithelioid cells, specifically located on the serous surface of the uterus and below the right appendix. The immunophenotype of the patient was positive for Vimentin, HMB45, TFE-3 and WT-1, but negative for SMA, S-100, CD10, CK, EMA, CD117, CD31 and Melan-A. Conclusion: PEComa is a rare mesenchymal tumor with benign manifestations. Pathological diagnosis should be combined with morphology and immunophenotype. The characteristic immunomarkers are HMB45, Melan-A and SMA. The understanding of clinical manifestations and pathologic features can improve the diagnosis and prevention of this type of tumor in female patients.

Keywords: Uterine neoplasm, PEComa, PEComas, histochemistry, diagnosis

Introduction

According to a new WHO classification of tumors in 2002, PEComa is a mesenchymal tumor consisting of perivascular epithelioid cells with unique histologic and immunohistochemical manifestations. It was first named by Zamboni et al in 1996 [1]. PEComa can occur anywhere in the body [2]; the uterus is the most common site of involvement except for the retroperitoneum. However, the tumors that occur in the uterus, cervix, gastrointestinal tract, kidney, liver, breast and lung are collectively referred to as PEComa-nos (PEComas) [3, 4]. They are so named because they do not meet any criteria for a normal disease entity as defined by histopathologic findings. The PEComas are omas of angiomyolipoma (AML), clear cell glioma of the lung (CCST), lymphangiomyolomatosis (LAM), clear cell myoblasts of the sickle ligament/ligament, and other rare clear cell tumors [5]. In this paper, a case of uterine PEComa obtained from clinical pathology examination in our hospital was reviewed, and relevant literature in recent years was reviewed to discuss the clinicopathologic characteristics, biological behavior determination and differential diagnosis of PEComas, so as to improve the understanding of this kind of tumor by pathologists.

Materials and methods

Clinical data

This case is from Department of Pathology, the First Affiliated Hospital of Bengbu Medical College. A 41-year-old woman was hospitalized for a week for pelvic mass found on physical examination. No family and clinical history of TSC. Color doppler ultrasound: irregular enlargement of uterus, 57 cm×90 cm×126 cm, multifocal substantial hypoechoic masses with right pelvic probe and below 4 cm×7.8 cm, fused into large sheets with a range of 7.4 cm×14 cm×13 cm, and substantial pelvic mass (uterine sar-

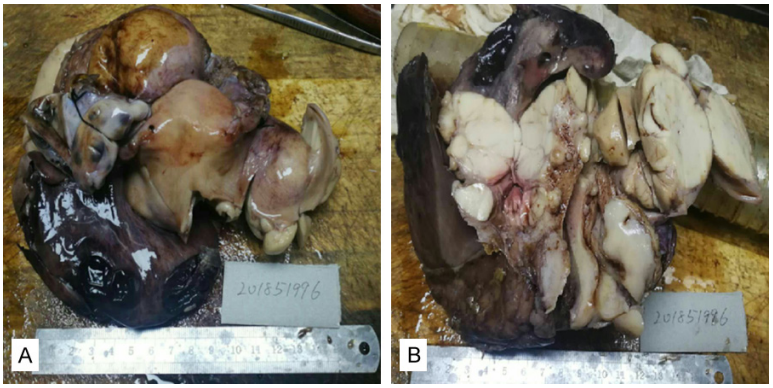

Figure 1. Gross appearance of uterine PEComa. A. The entire uterus was examined: irregular enlargement of uterus, 57 cm×90 cm×126 cm; B. More than ten tumors were seen in multiple sections of the uterus.

coma?). Pelvic CT: the right lower abdomen was occupied, and the enhanced scan was significantly enhanced. The possibility of mesenchymal tumor was considered. NET and solitary fibrious tumor needed to be ruled out, multifocal uterine fibroids were found, and no abnormality was found in five tumor samples. The patient underwent total abdominal hysterectomy and right adnexectomy.

Methods

Specimens of the lesion site after surgical resection were fixed with neutral 10% formalin, embedded with paraffin, and sectioned for H&E staining, and observed under a microscope. The paraffin sections of this specimen were stained by immunohistochemistry using the Elivision method according to the instructions. Antibodies HMB45, Melan-A, S-100, SMA, Desmin, Vimentin, Ki-67, EMA, CD56 and other markers were purchased from Fuzhou Maixin Biotechnology co., LTD., China.

Result determination

The immunohistochemical positive reaction was brownish yellow, of which HMB45, Melan-A [6], S-100 are the melanin cell markers [7], SMA, Desmin are muscle source sex markers, Vimentin for anaplastic spindle cell sarcoma component markers [8]. HMB-45, Melan-A, SMA positive signals were located in the cytoplasm, and Ki-67 tumor cell proliferation index (positioning the nucleus), can be more positive cells distributed in the area randomly selected 10 high field of vision, calculating the average positive cells in the tumor cells (%), as its proliferation index [9].

Results

Autopsy

The entire uterus was examined: the length from the cervix to the bottom of the uterus is 9 cm. Thickness of the endometrium was 0.1 cm, thickness of the muscular layer was 3 cm~4 cm, and the circumference of the cervix was 5.5 cm, which was smooth. More than ten tumors were seen in multiple sections of the uterus, with a length of 0.7 cm~4.5 cm, and a relatively tender texture. Right fallopian tube was 7 cm in length and 0.5 cm in circumference; Right ovary was 6 cm×4.5 cm×2 cm. 2 sacs were observed on the section surface of ovary. The length was 1 cm~1.5 cm, containing brown liquid. A neoplasm was seen on the serous membrane of the uterine body below the right adnexa, 19 cm×9 cm×4 cm, the cut surface was gray, slightly soft in texture, and some areas were dark red (**Figure 1A**, **1B**).

Microscopic examination

Tumor cells grew diffusely. Interstitial blood vessels were abundant, and some areas were large blood vessels. Most tumor cells were polygonal, with abundant cytoplasm resembling epithelial cells, with unclear cell boundaries. The cytoplasm was rich, eosinophilic, red and a few cytoplasm with clear cytoplasm. The distribution of chromatin in nucleus was uniform, the nuclear membrane was obvious, and nucleoli could be seen in some nuclei (**Figure 2A**, **2B**).

Immunohistochemical features

Results of immunohistochemical studies on paraffin block in the Department of Pathology, the First Affiliated Hospital of Bengbu Medical College: HMB45 (+) (**Figure 3A**), Vimentin (++) (**Figure 3B**), WT-1 (+) (**Figure 3C**), TFE-3 (+) (**Figure 3D**), SMA (-), S-100 (-), CD10 (-), H-caldesmon (-), CK (-), Melan-A (-), Ki-67 (+/-, <5%). Results of immunohistochemical markers of

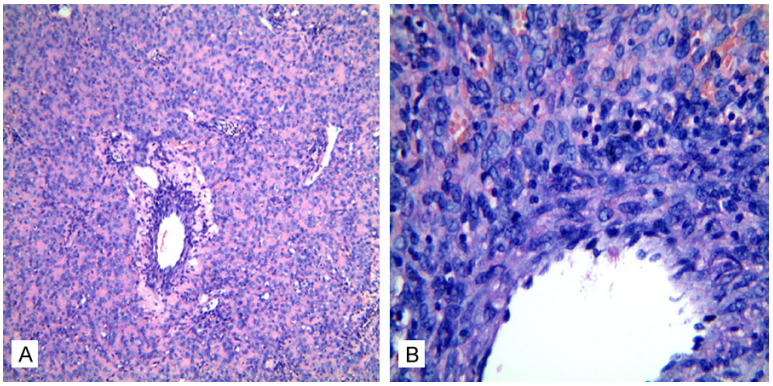

Figure 2. H&E stained photomicrograph of the tumor. A. Abundant interstitial vessels (H&E staining ×100). B. Most tumor cells are polygonal with abundant cytoplasm (H&E staining ×400).

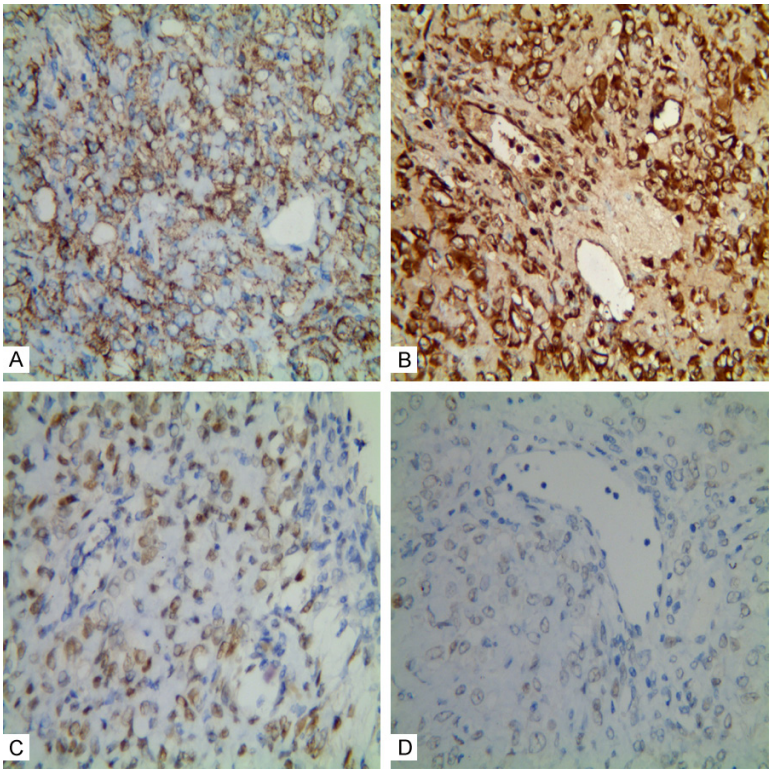

Figure 3. Immunohistochemical features of the tumor. Antibody expression was positive (magnification, ×400) (A-C). The expression of TTF-1 was negative (magnification, ×400) (D).

consultation in Tumor Hospital Affiliated to Fudan University: HMB45 (+), PNL2 (+), Desmin (+), TFE3 weak (+), ER (+), PR (+), CD10 (foci +), A103 (-), SMA (-), Caldesmon (-).

Pathologic diagnosis

According to the microscopic features and immunohistochemical markers, the tumor was diagnosed as Multifocal Perivascular Epithelioid Cell Tumor of the Uterus (PEComa).

Discussion

Histological origin and clinical features

Perivascular epithelioid cell tumor (PEComa) is a rare mesenchymal derived tumor subtype, originating in the perivascular epithelioid cell line [10]. PEComas have been reported in almost all tissues and organs of the body. Multifocal PEComa has been described in the literature, but its incidence is low. The uterus is the most common incidence site of PEComa in the female reproductive system, followed by gastrointestinal tract, urogenital tract and retroperitoneum, and the occurrence of soft tissue, skin and bone is relatively rare. Almost all reported cases of non-uterine PEComas are more common in women than in men, with a female-to-male ratio of up to 9:1, so hormones may be at least partially involved in their pathogenesis and/or phenotypic cellular presentation. The age of onset of the disease is broad, with a large proportion of young and middle-aged women. Patients diagnosed with PEComas range from 3 to 97 years old [11]. The uterus is the most common place of PEComas in the female reproductive system [5]. The age of onset of the patients is wide, and young and middle-aged women account for a large proportion. Due to the lack of non-specific clinical manifestations, it is difficult to diagnose the tumor early. Most of the cases had no obvious clinical symptoms, and a small number of patients were found to have non-specific symptoms such as irregular vaginal bleeding, abdominal pain, and compression syndrome due to

physical examination of other diseases. The size of the mass is usually 2~5 cm, but it can be more than 10 cm. Preoperative imaging examination shows no specificity, such as leiomyoma or lobulated heterogeneous endometrial stromal sarcoma, which is also a diagnostic challenge for radiologists [12]. About 10% of PEComas are associated with autosomal dominant tuberous sclerosis complex (TSC), and this patient has no history of tuberous sclerosis [11, 13].

Pathologic features

The tumor generally has no obvious characteristic manifestations, and most of the tumors are masses with clear boundaries or the formation of pseudomembrane, and some cases may be accompanied by cystic changes. The diagnosis of PEComas has no clear imaging features [14]. Histologically, perivascular epithelioid cells show clear or granular cytoplasm and central rounded nuclei, with no prominent nucleoli. Immunohistochemical staining of the tumor cells showed positive for HMB-45, indicating that the tumor cells had melanocyte characteristics, in addition to expressing smooth muscle markers, occasionally positive for S-100, SMA and junction protein, but negative for epithelial and endocrine markers [15, 16].

Differential diagnosis

1. Malignant melanoma: Tumor cell atypia in PEComas is not obvious, mitotic appearance is rare, and S-100 protein is generally not expressed [17]; 2. Soft tissue clear cell tumor: this tumor has no characteristic surrounding vascular phenomenon, and does not express SMA [18]; 3. Epithelioid leiomyoma: composed of spindle and/or epithelioid cells that respond to smooth muscle markers, such as SMA, but are insensitive to melanocyte markers [1]; 4. Endometrial stromal sarcoma: PEComas cells are large and round or polygonal with abundant eosinophil cytoplasm and are HMB45 positive; However, the tumor cells are spindle shaped with less cytoplasm, and HMB45 is negative [19]; 5. Clear cell carcinoma of uterus (UCC): the tumor cells has clear cytoplasm and are composed of hobnail cells, forming solid cells, which are negative with HMB45 and positive with CK [20]; 6. Paraganglioma: when the cytoplasm is clear, it should be distinguished from PEComas. The accessory ganglion cells are arranged into stripes, glands or nests, surrounded by flat supporting cells, and organoid and prosthesis structure is obvious. In addition, HMB45 is negative; NSE, Syn, CgA and NF are positive, and S-100 protein is positive in Sertoli cells [21].

Benign and malignant criteria

Due to the rarity of PEComa, its biological behavior cannot be determined, and there are no clear diagnostic criteria for malignant PEComa, malignant PEComa Folpe, et al in 2005 after studying 26 cases of soft tissue and female genital tract PEComa with follow-up consider that malignant PEComa should have the following features: the tumor >5 cm in diameter, with invasive growth pattern, high nuclear size, cell necrosis, mitosis >1/50 HPF and poor clinical behavior. Most pathologists agree that this standard is a practical way to diagnose malignant PEComa, but it remains to be proven [22].

Conclusion

PEComa is a heterogeneous and usually benign tumor that generally has a good prognosis. Malignant cases are rare and often present as local recurrence and distant metastasis. Currently, there is no standardized treatment mode for primary PEComa local recurrence and metastasis. Surgical resection is now the first choice, and radical hysterectomy with bilateral salpingectomy is the best surgical method for the uterine PEComa [23]. Generally, there is no recurrence after surgical resection, and the effect of radiotherapy and chemotherapy is not obvious. Recently, some studies have reported certain effects of oral administration of sirolimus, an mTOR inhibitor [23, 24], on malignant PEComas, suggesting that sirolimus appears to be adjunctive therapy for PEComa. Due to the small number of cases of this disease, its tissue origin and pathogenesis are still unclear, so whether PEComa is an independent disease has not been determined. However, with the increasing number of reports and studies, pathologic character-based diagnosis is becoming more clear, which may provide information for correct treatment and help patients to obtain early diagnosis and better treatment.

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The case report and published written informed consent were obtained from the patient.

Disclosure of conflict of interest

None.

Abbreviations

PEComa, tumor with pervascular epithelioid cells; PEComas, PEComa-nos.

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